



# TRANSMITTAL FORM

Application Serial Number	10/759,374
Filing Date	January 16, 2004
First Named Inventor	Hafeman
Group Art Unit	Not yet assigned
Examiner Name	Not yet assigned
Attorney Docket No.	THI-003
Patent No.	Not applicable
Issue Date	Not applicable

## ENCLOSURES (check all that apply)

<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Check Attached <input type="checkbox"/> Copy of Fee Transmittal Form <input type="checkbox"/> Amendment/Response <input type="checkbox"/> Preliminary <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Letter to Official Draftsperson including Drawings [Total Sheets ____] <input type="checkbox"/> Petition for Extension of Time <input checked="" type="checkbox"/> Information Disclosure Statement <input checked="" type="checkbox"/> Form PTO-1449 <input checked="" type="checkbox"/> Copies of IDS Citations <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Sequence Listing submission <input type="checkbox"/> Paper Copy/CD <input type="checkbox"/> Computer Readable Copy <input type="checkbox"/> Statement verifying identity of above	<input type="checkbox"/> Copy of Notice to File Missing Parts of Application <input type="checkbox"/> Formal Drawing(s) <input type="checkbox"/> Request For Continued Examination (RCE) Transmittal <input type="checkbox"/> Power of Attorney (Revocation of Prior Powers) <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Executed Declaration and Power of Attorney for Utility or Design Patent Application <input type="checkbox"/> Small Entity Statement <input type="checkbox"/> CD(s) for large table or computer program <input type="checkbox"/> Amendment After Allowance <input type="checkbox"/> Request for Certificate of Correction <input type="checkbox"/> Certificate of Correction (in duplicate)	<input type="checkbox"/> Notice of Appeal to Board of Patent Appeals and Interferences <input type="checkbox"/> Appeal Brief (in triplicate) <input type="checkbox"/> Status Inquiry <input checked="" type="checkbox"/> Return Receipt Postcard <input checked="" type="checkbox"/> Certificate of First Class Mailing under 37 C.F.R. 1.8 <input type="checkbox"/> Certificate of Facsimile Transmission under 37 C.F.R. 1.8 <input type="checkbox"/> Additional Enclosure(s) (please identify below)
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## CORRESPONDENCE ADDRESS

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## SIGNATURE BLOCK

Respectfully submitted,

Date: March 15, 2004  
Reg. No. 44,381  
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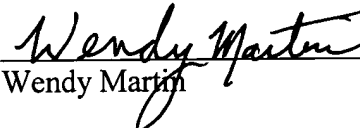
PATENT  
Attorney Docket No. THI-003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Hafeman  
SERIAL NO.: 10/759,374 GROUP NO.: Not yet assigned  
FILING DATE: January 16, 2004 EXAMINER: Not yet assigned  
TITLE: METHODS AND DEVICES FOR MONITORING CELLULAR  
METABOLISM IN MICROFLUIDIC CELL-RETAINING  
CHAMBERS

**CERTIFICATE OF FIRST CLASS MAILING UNDER 37 C.F.R. 1.8**

I hereby certify that this correspondence, and any document(s) referred to as enclosed herein, is/are being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 15<sup>th</sup> day of March, 2004.

  
Wendy Martin

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith are: Transmittal Form (1 page); Information Disclosure Statement (2 pages); Form PTO-1449 (5 pages); References Labeled A1 to A26, B1 to B8 and C1 to C39; and a return receipt postcard.



PATENT  
Attorney Docket No. THI-003

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT(S): Hafeman  
SERIAL NO.: 10/759,374 GROUP NO.: Not yet assigned  
FILING DATE: January 16, 2004 EXAMINER: Not yet assigned  
TITLE: METHODS AND DEVICES FOR MONITORING CELLULAR  
METABOLISM IN MICROFLUIDIC CELL-RETAINING  
CHAMBERS

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

Sir:

In accordance with the provisions of 37 C.F.R. 1.97 and 1.98, Applicants hereby make of record the patents and publications listed on the accompanying Form PTO-1449, and other information contained herein, for consideration by the Examiner in connection with the examination of the above-identified patent application. Copies of the patents and publications are enclosed.

**REMARKS**

In accordance with the provisions of 37 C.F.R. 1.97, this statement is being filed (CHECK ONE):

- ☒ (1) within three (3) months of the **filing date** of a national application other than a continued prosecution application under 37 C.F.R. 1.53(d), or within three (3) months of the **date of entry of the national stage** as set forth in 37 C.F.R. 1.491 in an international application, or before the mailing of the **first Office action** on the merits, or before the mailing of a **first Office action** after the filing of a request for continued examination under 37 C.F.R. 1.114; or
- ☐ (2) after the period defined in (1) but before the mailing date of a **final action** or a **notice of allowance** under 37 C.F.R. 1.311, and
- ☐ the requisite Statement is below, **OR**
- ☐ the requisite fee under 37 C.F.R. 1.17(p), namely **\$180.00**, is included herein, or

- ☐ (3) after the mailing date of a **final action** or **notice of allowance** but before the payment of the **issue fee**, **AND**
- ☐ the requisite Statement is below, **AND**
- ☐ the requisite petition fee under 37 C.F.R. 1.17(p), namely **\$180.00** is included herein.

In addition, Applicant wishes to inform the Examiner about the following co-pending patent applications, and Office Actions issued therein:

U.S. Serial No. 10/313,917, filed on December 6, 2002, by Neilson *et al.* (THI-001); and  
U.S. Serial No. 10/688,791, filed on October 17, 2003, by Teich *et al.* (THI-002).

It is respectfully requested that each of the patents and publications listed on the attached Form PTO-1449, and other information contained herein, be made of record in this application.

Respectfully submitted,

Date: March 15, 2004  
Reg. No. 44,381

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VER 12/00  
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FORM PTO - 1449

## INFORMATION DISCLOSURE STATEMENT

ATTY DOCKET NO.: THI-003

APPLICANTS: Hafeman

SERIAL NO.: 10/759,374

FILING DATE: January 16, 2004

GROUP: Not yet assigned

## U.S. PATENT DOCUMENTS

EXAM. INIT.		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
	A1	4,711,851	12/08/1987	McNamara et al.			
	A2	5,104,804	04/14/1992	Humphries et al.			
	A3	5,278,048	01/11/1994	Parce et al.			
	A4	5,468,605	11/21/1995	Harris et al.			
	A5	5,495,850	03/05/1996	Zuckerman			
	A6	5,496,697	03/05/1996	Parce et al.			
	A7	5,536,662	07/16/1996	Humphries et al.			
	A8	5,567,598	10/22/1996	Stitt et al.			
	A9	5,766,875	06/16/1998	Hafeman et al.			
	A10	5,774,214	06/30/1998	Prettyjohns			
	A11	5,792,426	08/11/1998	Portman et al.			
	A12	5,830,138	11/03/1998	Wilson			
	A13	5,959,297	09/28/1999	Weinberg et al.			
	A14	5,998,517	12/07/1999	Gentle et al.			
	A15	6,030,917	02/29/2000	Weinberg et al.			
	A16	6,080,574	06/27/2000	Berndt			
	A17	6,380,605	04/30/2002	Verhaegen			
	A18	6,395,506	05/28/2002	Pitner et al.			
	A19	6,395,555	05/28/2002	Wilson et al.			
	A20	2002-0098592 A1	07/25/2002	Neilson			
	A21	2002-0098593 A1	07/25/2002	Neilson			
	A22	2002-0132360 A1	09/19/2002	Neilson			
	A23	2002-0146345 A1	10/10/2002	Neilson			
EXAMINER				DATE CONSIDERED			

<b>FORM PTO - 1449</b>				<b>ATTY DOCKET NO.:</b> THI-003					
<b>INFORMATION DISCLOSURE STATEMENT</b>				<b>APPLICANTS:</b> Hafeman					
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				<b>FILING DATE:</b> January 16, 2004					
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<b>U.S. PATENT DOCUMENTS</b>									
<b>EXAM. INIT.</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>NAME</b>	<b>CLASS</b>	<b>SUB CLASS</b>	<b>FILING DATE IF APPROPRIATE</b>		
	A24	2002-0146836 A1	10/10/2002	Neilson					
	A25	2003-0059807 A1	03/27/2003	Longmont et al.					
	A26	6,673,532	01/06/2004	Rao					
<b>FOREIGN PATENT DOCUMENTS</b>									
<b>EXAM. INIT.</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>COUNTRY CODE</b>	<b>CLASS</b>	<b>SUB CLASS</b>	<b>FILING DATE</b>	<b>ABSTRACT ONLY</b>	<b>ENGLISH LANG (Y/N)</b>
	B1	WO 00/32308	06/08/2000	PCT				NO	YES
	B2	WO 00/36410 A1	06/22/2000	PCT				NO	YES
	B3	WO 01/85901 A2	11/15/2001	PCT				NO	YES
	B4	WO 01/85901 A3	11/15/2001	PCT				NO	YES
	B5	WO 02/08385	01/31/2002	PCT				NO	YES
	B6	WO 02/11881 A1	02/14/2002	PCT				NO	YES
	B7	WO 02/083852	05/2002	PCT				NO	YES
	B8	WO 02/099386 A2	12/12/2002	PCT				NO	YES
<b>OTHER ART, JOURNAL ARTICLES, ETC.</b>									
<b>EXAM. INIT.</b>	<b>OTHER DOCUMENTS: (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>								
	C1	Beebe D.J., Mensing G.A., Walker G.M. (2002) "Physics and applications of microfluidics in biology." <u>Annu. Rev. Biomed. Eng.</u> , 4, 261-86							
	C2	Beebe D.J., Moore J.S., Bauer J.M., Yu Q., Liu R.H., Devadoss, C., Jo B.H. (2000) "Functional hydrogel structures for autonomous flow control inside microfluidic channels. <u>Nature</u> , 404, 588-90							
	C3	Bousse, L., Cohen, C., Nikiforov, T., Chow, A., Kopf-Sill, A.R., Dubrow, R. and Parce, J.W. (2000) "Electrokinetically Controlled Microfluidic Analysis Systems." <u>Annu. Rev. Biophys. Biomol. Struct.</u> 29, 155-181							
	C4	Brecht & Gauglitz, "Optical probes and transducers," Biosensors and Bioelectronics, 10, p. 923-936, 1995							
<b>EXAMINER</b>					<b>DATE CONSIDERED</b>				

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	C5	Clark, L.C. <i>Inr. Ann. NY Acad. Sci.</i> 1962; 102:29-45
	C6	B. Cunningham, P. Li, B. Lin, J. Pepper, "Colorimetric resonant reflection as a direct biochemical assay technique," <i>Sensors and Actuators B</i> , Volume 81, p. 316-328, Jan. 5, 2002
	C7	Flora K and J Brennan. Comparison of Formats for the Development of Fiber-Optic Biosensors Utilizing Sol-Gel Derived Materials Entrapping Fluorescently-Labeled Proteins. <i>Analyst</i> , 1999, 124, 1455-146
	C8	Ge X, Kostov Y, and G Rao. High Stability non-invasive autoclavable naked optical CO <sub>2</sub> sensor. 2003. <i>Biosensor and Bioelectronics</i> 18:pp.857-865
	C9	Gesinski RM, Morrison JH, Toepfer JR. "Measurement of oxygen consumption of rat bone marrow cells by a polarographic method." <i>J Appl Physiol.</i> 1968; 24(6):751-754
	C10	Hasselbrink E.F. Jr., Shepodd T.J., Rehm J. (2002) "High-pressure microfluidic control in lab-on-a-chip devices using mobile polymer monoliths." <i>Anal Chem.</i> 74, 4913-8
	C11	Hua S.Z., Sachs F., Yang D.X., Chopra H.D. (2002) "Microfluidic actuation using electrochemically generated bubbles." <i>Anal Chem.</i> 74, 6392-6
	C12	Huber et al., "Direct optical immunosensing (sensitivity and selectivity)," <i>Sensors and Actuators B</i> , 6, p. 122-126, 1992
	C13	Jin et al., "A biosensor concept based on imaging ellipsometry for visualization of biomolecular interactions," <i>Analytical Biochemistry</i> , 232, p. 69-72, 1995
	C14	Jordan & Corn, "Surface Plasmon Resonance Imaging Measurements of Electrostatic Biopolymer Adsorption onto Chemically Modified Gold Surfaces," <i>Anal. Chem.</i> , 69:1449-1456 (1997)
	C15	Lähdesmäki I, Scampavia LD, Beeson C, and Ruzicka J. "Detection of Oxygen Consumption of Cultured Adherent Cells by Bead Injection Spectroscopy." <i>Anal. Chem.</i> 1999; 71: 5248-5252
	C16	Lehmann, M, Baumann W, Brischwein M, Gahle H-J, Freund I, Ehret R, Dreschler S, Palzer H, Kleintges M, Sieben U and Wolf B. "Simultaneous measurement of cellular respiration and acidification with a single CMOS ISFET. 2001." <i>Biosensors &amp; Bioelectronics.</i> 2001;16:195-203
	C17	McConnell, H.M., Owicki, J.C., Parce, J.W., Miller, D.L., Baxter, G.T., Wada, H.G. and Pitchford, S. (1992) "The Cytosensor Microphysiometer: Biological Applications of Silicon Technology" <i>Science</i> 257: 1906
	C18	Metzgar, R., Deglmann, C.J., Hoerrlein, S., Zapf, S. and Hilfrich, J. (2001) <i>Toxicology</i> 166, 97-108
	C19	Morhard et al., "Immobilization of antibodies in micropatterns for cell detection by optical diffraction," <i>Sensors and Actuators B</i> , 70, p. 232-242, 2000

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EXAM. INIT.	OTHER DOCUMENTS: (Including Author, Title, Date, Relevant Pages, Place of Publication)		
	C20	Matterlini et. al., "Depression of Endothelial and Smooth Muscle Cell Oxygen Consumption by Endotoxin," American Journ. of Physio. vol. 275, No. 168 p. 776-782, Sep. 1998	
	C21	O'Riordan TC, Buckley D., Ogurtsov V, O'Connor R., Papkovsky DB "A cell viability assay based on monitoring respiration by optical oxygen sensor." <i>Anal. Biochem.</i> 2000; 278(2):221-227	
	C22	Owicki, J.C., Bousse, L.J., Hafeman, D.G., Kirk, G.L., Olson, J.D., Wada, H.G. and Parce, J.W. (1994) "The Light-Addressable Potentiometric Sensor: Principles and Biological Applications." <i>Ann. Rev. Biophys. Biomol. Struct.</i> 23: 87	
	C23	Panten U and Klein H. "O <sub>2</sub> consumption by isolated pancreatic islets, as measured in a Microincubation system with a Clark-type electrode." <i>Endocrinology</i> 1982; 111:1595-1600	
	C24	Parce W, Owicki J, Kercso K, Sigal G, Wada H, Muir V, Bousse L, Ross K, Sikic B, and McConnell H. 1989. "Detection of Cell-Affecting Agents with a Silicon Biosensor." <i>Science</i> . 1989; 246(4927):243-247	
	C25	Pattison R, Swamy J, Mendenhall B, Hwang C, and Frohlich B. "Measurement and Control of Dissolved Carbon Dioxide in Mammalian Cell Culture Processes Using an in Situ Fiber Optic Chemical Sensor." 2000. <i>Biotechnology Prog.</i> 16:769-774	
	C26	Pouli, A.E., Karagenc, N., Arden, S., Bright, N., Schofield, G.S., Hutton, J.C. & Rutter, G.A. (1998) "A phogrin-aequorin chimaera to image Ca <sup>2+</sup> in the vicinity of secretory granules." <i>Biochem. J.</i> 330, 1399 - 1404	
	C27	Robiolio et al., "Oxygen diffusion and mitochondrial respiration in neuroblastoma cells," <i>Am. J. Physiol.</i> 256 (6 Pt 1):C1207-1213 (Jun. 1989)	
	C28	Rumsey et al., "Cellular Energetics and the Oxygen Dependence of Respiration in Cardiac Myocytes Isolated from Adult Rat" <i>Journal of Biological Chemistry</i> . 265(5):15392-15399. 1990	
	C29	Shenoy MA, Biaglow JE, Varnes ME, Hetzel FW. "Inhibition of cultured human tumor cell oxygen utilization by chlorpromazine." <i>Adv Exp Med Biol.</i> 1983;159:359-68	
	C30	Thorsen, T., Maerkl, S.J. and Quake, S.R. (2002) Microfluidic Large-Scale Integration <i>Science</i> 298, 580-586	
	C31	Tolosa L, Kostov Y, Harms P, Rao G. "Noninvasive measurement of dissolved oxygen in shake flasks." <i>Biotechnol Bioeng</i> 2002 Dec 5;80(5):594-7	
	C32	Unger, M.A., Chou, H-P, Thorsen, T., Scherer, A, and Quake, S.R. (2000) <i>Science</i> 288, 113	
	C33	Vanderkooi et. al., "An Optical Method for Measurement of Dioxygen Concentration Based upon Quenching of Phosphorescence," <i>J. Biol. Chem.</i> , 262 (12):5476-5482 (Apr. 1987)	



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<b>EXAM. INIT.</b>	<b>OTHER DOCUMENTS: (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>		
	C34	Wada, H.G. Indelicato, S.R., Meyer, L. Kitamura, T., Miyajima, A., Kirk, G., Muir, V.C. and Parce, J.W. (1993) "GM-CSF Triggers a Rapid Glucose Dependent Extracellular Mediated Activation of Acid Production." <i>J. Cell Physiol.</i> 154: 129	
	C35	Wiley, C and Beeson, C. (2002) "Continuous measurement of glucose utilization in heart myoblasts." <i>Analytical Biochemistry</i> 304, 139-146	
	C36	Wilson et al., "The Oxygen Dependence of Mitochondrial Oxidative Phosphorylation Measured by a New Optical Method for Measuring Oxygen Concentration," <i>J. Biol. Chem.</i> , 263:2712-2718 (1988)	
	C37	Wodnicka M, Guarino RD, Hemperly JJ, Timmins MR, Stitt D, Pitner JB. "Novel fluorescent technology platform for high throughput cytotoxicity and proliferation assays." <i>Journal of Biomolecular Screening</i> . 2000; 5:141-152	
	C38	Wolfbeis OS, 2002. "Fiber-Optic Chemical Sensors and Biosensors." <i>Annal of Chem.</i> 2002; 74:2663-2678	
	C39	Handbook of Fluorescent Probes and Research Products published by Molecular Probes, Inc., Eugene, Oregon, USA, <a href="http://www.probes.com/handbook/">http://www.probes.com/handbook/</a> (accessed 3/12/04), Table of Contents, 2 pages	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	